

DATE: August 4, 1978

SUBJECT: Roundup - glyphosate Evaluation of Validation of IBT J-565;
BTL 71-33; Two year chronic oral toxicity study with CP67573
in Beagle Dogs. EPA Reg. #528-308 - Caswell #661A

FROM: William Dykstra, Ph.D.
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TO: Robert Taylor (PM #25)
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Registrant: Monsanto Agricultural Products
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Recommendation

The validated report does not adversely impact on original TOX review. The NEL is greater than 300 ppm in the diet of beagle dogs for 2 years.

Review:

A. Original review; PP 5F1536, Diana Reisa, Ph.D.

Four males and four females were assigned to the control group and to each of the three experimental groups (30, 100 and 300 ppm). The following parameters were monitored and found not to be significantly different from controls; body weight, food consumption, behavioral reaction, mortality, hematological studies, blood chemistry, urinalyses, organ weights, gross pathology, histopathology. The following studies were conducted upon each dog from the control and experimental groups just prior to the inception of the study and after 3, 6, 9, 12, 18 and 24 months of testing and were comparable to controls:

Hematology - WBC, RBC, hematocrit, and differential leukocyte count

Blood Chemistry - BUN, glucose, SAP, SGOT, SGPT

Urinalysis - albumin, glucose, pH microscopic elements

At the conclusion of the study, the dogs from each group were sacrificed and all major tissues and organs were examined grossly.

Organ weights - liver, kidneys, heart, brain, spleen, gonads, adrenal glands, thyroid, pituitary and testes

Histology (Craig Fischer, D.V.M., Veterinary Pathologist).

The following were examined histologically (H&E stain): adrenal glands, aorta (thoracic), bone marrow (sternum), brain (cerebrum, cerebellum, pons) caecum, colon, esophagus, gall bladder, gonads, heart, kidneys, liver, lungs, cervical and mesenteric lymph nodes, skeletal muscle, pancreas, sciatic nerve, pituitary, prostate, submaxillary gland, small intestine, spinal cord, spleen, stomach, trachea, thyroid, uterus, urinary bladder. The histological changes in the above tissues were not compound-related and were compatible with lesions normally seen in dogs maintained under laboratory conditions. The NEL for this study is in excess of 300 ppm.

B. Package of materials relating to validation

1. Certification statement signed Monte C. Throdahl, Monsanto Co.
2. Exhibit A - Biography of G.L. Wesp
3. Exhibit B - Biography of G.J. Levinskas
4. Exhibit C - Biography of D.W. Fassett
5. Exhibit D - Audit Statement of G.L. Wesp

I. Body wt. Data

Minor discrepancies which do not impact adversely on original TOX review.

II. Food Consumption

Minor discrepancies have no impact adversely on original TOX review

III. Hematology

Minor discrepancy which does not adversely impact on original TOX review

IV. Blood Chemistry

Minor discrepancies which do not adversely impact on original TOX review

V. Urinalyses

Minor discrepancies which do not adversely impact on original TOX review

VI. Organ Weights

Four errors which do not adversely impact on original review

VII. Gross and Histopathology

2 minor discrepancies which do not adversely impact on original TOX review.

Conclusion: Validated Report does not adversely impact on original TOX review.

6. Exhibit E - Validation Statement of D.W. Fassett

7. Exhibit F - Responses to EPA questions

8. Exhibit G - Stability reports - do not adversely impact on TOX review

9. Marked Copy of IBT Report No. 651-565 showing discrepancies

R/D Initialed: REngler 8/4/78
WDykstra/ccw

8/28/78